

REMARKS

Status of the Prosecution

Claims 45, 55-65, 70-78, and 80 are pending in the application, and were examined. All previous rejections under 35 U.S.C. §§ 112, 102(b) and 103(a) were withdrawn. Claim 45 currently stands objected to for informalities. Claims 45, 55-65, 70-78, and 80 are newly rejected under 35 U.S.C. Section 103(a), as follows.

Claims 45, 55-58, and 70-78 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over any one of (1) Srivastava et al. (1997, Carcinogenesis 18: 1799-1808); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347).

Claims 45, 55-58, 60-64, and 70-76 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over any one of (1) Srivastava et al. (1997), (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347) in view of Grattarola (1976, J. Natl. Cancer Inst. 56: 11-16).

Claims 45, 55-58, 59, and 70-76 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over any one of (1) Srivastava et al. (1997); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347) in view of Silverstein et al. (1994, Cancer 73: 1673-1677, abstract only).

Claims 45, 55-58, 65, and 70-76 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over any one of (1) Srivastava et al. (1997); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347), in view of Mgbonyebi et al. (1997, Proc. Ann. Meeting Am. Soc. Cancer Res. pp A1977 XP002109660).

Claims 45, 55-58, 70-76, and 77 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over any one of (1) Srivastava et al. (1997); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347), in view of Saal et al. (1991 Fert. Steril. 56:225-9).

Claims 45, 55-58, 70-76, and 78 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over any one of (1) Srivastava et al. (1997); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347), in view

of any one of (1) Platanius et al. (1998, J. Biol. Chem. 273: 5577-5581); (2) Oberg et al. (1989, J. Natl. Cancer Inst. 81: 531-535); (3) Recchia et al. (1998, Clin. Ter. 149: 203-208) or (4) Robinson et al. (1990, Breast Cancer Res. Treat. 15: 95-101).

Claims 45, 55-58, 70-76, and 80 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over any one of (1) Srivastava et al. (1997); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347), in view of the Sigma Chemical Co. catalog (1995, page 263).

Claims 61 and 62 are cancelled herein without prejudice. The limitations of claim 62 have been incorporated into the base claim. Applicants reserve the right to pursue the subject matter cancelled from claim 61 at a later time. Claim 45 is amended herein, to more clearly define the method of the invention. Support for the amendment to claim 45 may be found throughout the specification, for example, at page 10, lines 17-23 and 24-31, and Examples 1 and 2. Thus, no new matter has been added by way of these amendments. Applicants respectfully submit that the presently amended claims are in condition for allowance, for the reasons set forth below.

Claim 45 Meets all Formal Requirements

Claim 45 is objected to for informalities. Specifically, lines 4 and 5 of claim 45 recite "hGC" instead of hCG. Claim 45 is amended herein to recite "hCG" instead of "hGC," thereby correcting the informality. Applicants respectfully request reconsideration and withdrawal of the objection.

The Claims are Directed to Non-Obvious Subject Matter

Claims 45, 55-58, and 70-76 are rejected under 35 U.S.C. Section 103(a) as allegedly obvious over any one of Srivastava et al. (Carcinogenesis, 18:1799-1808 (1997)), Russo et al. (J. Natl. Cancer Inst., 82:1286-7 (1990)), or Russo et al. (Br. J. Cancer, 62:2343-7 (1990)). The Office Action alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to treat clinically manifest mammary tumors because any of the three references teach how to obtain hCG and how to administer the active ingredient *in vivo*, based on the dosage schedules for the animal models, as set forth in the references. Specifically, the Office Action alleges that Srivastava et al. teach the invention through the

statement “the use of agents like hCG that induce apoptosis may constitute a useful approach for the prevention and therapy of breast cancer.” Applicants traverse the rejection as applied to the currently amended claims.

In order for a *prima facie* case of obviousness to be established under 35 U.S.C. §103, there must be a motivation in the art to modify or combine the references identified by the examiner, there must be a reasonable expectation of success, not merely an invitation to experiment, and the prior art references must teach or suggest all limitations of the claims. Moreover, the mere fact the references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. (MPEP 2143.01).

Claim 45 now calls for a method of treating clinically manifest mammary tumors in postmenopausal women. The Srivastava and Russo references disclose data obtained in a rat model of breast cancer. None of these references, alone or in combination, teach or suggest a method of treating clinically manifest mammary tumors in postmenopausal women by detecting the mammary tumor in a host, then initiating and carrying out a dosing regimen of hCG in amounts and for a time effective to inhibit mammary tumor cell proliferation. The statement by Srivastava et al. that “the use of agents like hCG that induce apoptosis *may* constitute a useful approach for the prevention and therapy of breast cancer” constitutes merely an invitation to experiment, and does not teach or suggest the method as presently claimed, with all limitations, nor impart any expectation of success in practicing the claimed method. Indeed, when the currently claimed invention is considered as a whole, none of the cited references provide the requisite teaching or suggestion of the invention. Further, there is nothing in any of the references to motivate the skilled artisan to modify or combine any teaching of these references to arrive at a method of treating clinically manifest tumors in post-menopausal women. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 45, 55-58, and 70-76 under 35 U.S.C. Section 103(a).

Claims 45, 55-58, 60-64, and 70-76 are rejected under 35 U.S.C. §103(a) as allegedly obvious over any one of (1) Srivastava et al. (1997, Carcinogenesis 18: 1799-1808); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347) in view of Grattarola (1976, J. Natl. Cancer Inst. 56: 11-16). The Office Action alleges that, although the primary references do not teach metastatic mammary

tumors, clinically manifest mammary tumors in pre- or postmenopausal women, or administering hCG to a host with at least one other treatment, Grattarola teaches a method of administering 15,000 IU hCG to advanced breast cancer patients who are pre- or postmenopausal women and had undergone surgery, and that it would therefore have been obvious to combine the teachings of Grattarola with the primary references to arrive at the invention as claimed. Applicants traverse the rejection.

Grattarola discloses the administration of 15,000 IU hCG to breast cancer patients that “were free of any recurrence” of the disease. (see, e.g., Grattarola Abstract). In contrast, the claims of the present invention are directed to methods to treat postmenopausal women who have a clinically manifest mammary tumor, that is, treating patients who are not free of recurrence. In addition, Grattarola teaches the administration of hCG to stimulate testosterone production following ovariectomy in breast cancer patients. (see, e.g., page 11, right hand column, third complete paragraph). Grattarola does not teach nor suggest the possibility for using hCG as a treatment for clinically manifest breast cancer tumors in postmenopausal women.

Thus, all of the limitations of the invention are neither taught nor suggested by the prior art, alone or in combination. In this regard, the skilled artisan would not be motivated to modify or combine any of these references, and would not have an expectation of success to arrive at the invention as claimed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 45, 55-58, 60-64, and 70-76 under 35 U.S.C. Section 103(a).

Claims 45, 55-58, 59, and 70-76 are rejected under 35 U.S.C. §103(a) as allegedly obvious over any one of (1) Srivastava et al. (1997, Carcinogenesis 18: 1799-1808); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347) in view of Silverstein et al. (1994, Cancer 73: 1673-1677, abstract only). The Office Action alleges that although the primary references do not teach or suggest that hCG is effective as a treatment against tubular or lobular mammary carcinoma, Silverstein teaches that tubular or lobular invasive breast mammary carcinoma are forms of breast cancer, and that it would have been obvious to use the methods of the present invention to treat patients with these specific stages of the disease. Applicants traverse the rejection.

As set forth above, the present invention is directed to a method of treating clinically manifest mammary tumors in postmenopausal women, and the primary references do not teach or suggest this method. The deficiencies in the primary references are not supplied by Silverstein. Silverstein does not teach or suggest that hCG could be used to treat clinically manifest tubular or lobular invasive carcinoma in postmenopausal women. Thus, all of the limitations of the invention are not taught or suggested by the prior art, alone or in combination. In this regard, the skilled artisan would not be motivated to modify or combine any of these references, and would not have an expectation of success to arrive at the invention as claimed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 45, 55-58, 59, and 70-76 under 35 U.S.C. Section 103(a).

Claims 45, 55-58, 65, and 70-76 are rejected under 35 U.S.C. §103(a) as allegedly obvious over any one of (1) Srivastava et al. (1997, Carcinogenesis 18: 1799-1808); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347), in view of Mgbonyebi et al. (1997, Proc. Ann. Meeting Am. Soc. Cancer Res. pp A1977 XP002109660). The Office Action alleges that although the primary references do not teach or suggest that hCG is effective as a treatment for estrogen positive mammary tumors, Mgbonyebi teaches that hCG is effective in inhibition of estrogen positive breast cancer cells, and that it would have been obvious to use the methods of the present invention to treat patients with estrogen positive breast cancer cells. Applicants traverse the rejection.

As set forth above, the present invention is directed to a method of treating clinically manifest mammary tumors in postmenopausal women, and the primary references do not teach or suggest this method. The deficiencies in the primary references are not supplied by Mgbonyebi. Mgbonyebi does not teach or suggest that hCG could be used to treat clinically manifest estrogen positive breast cancer in postmenopausal women. Thus, all of the limitations of the invention are not taught or suggested by the prior art, alone or in combination. In this regard, the skilled artisan would not be motivated to modify or combine any of these references, and would not have an expectation of success to arrive at the invention as claimed. Accordingly, Applicants respectfully request reconsideration and

withdrawal of the rejection of claims 45, 55-58, 65, and 70-76 under 35 U.S.C. Section 103(a).

Claims 45, 55-58, 70-76, and 77 are rejected under 35 U.S.C. §103(a) as allegedly obvious over any one of (1) Srivastava et al. (1997, Carcinogenesis 18: 1799-1808); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347), in view of Saal et al. (1991 Fert. Steril. 56:225-9). The Office Action alleges that although the primary references do not teach or suggest injecting hCG subcutaneously, Saal teaches the administration of hCG subcutaneously, and that it would have been obvious to administer hCG subcutaneously in the methods of the present invention. Applicants traverse the rejection.

As set forth above, the present invention is directed to a method of treating clinically manifest mammary tumors in postmenopausal women, and the primary references do not teach or suggest this method. The deficiencies in the primary references are not supplied by Saal. Saal does not teach or suggest that hCG could be administered subcutaneously to treat clinically manifest mammary tumors in postmenopausal women. Thus, all of the limitations of the invention are not taught or suggested by the prior art, alone or in combination. In this regard, the skilled artisan would not be motivated to modify or combine any of these references, and would not have an expectation of success to arrive at the invention as claimed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 45, 55-58, 70-76, and 77 under 35 U.S.C. Section 103(a).

Claims 45, 55-58, 70-76, and 78 are rejected under 35 U.S.C. §103(a) as allegedly obvious over any one of (1) Srivastava et al. (1997, Carcinogenesis 18: 1799-1808); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347), in view of any one of (1) Plantanias et al. (1998, J. Biol. Chem. 273: 5577-5581); (2) Oberg et al. (1989, J. Natl. Cancer Inst. 81: 531-535); (3) Recchia et al. (1998, Clin. Ter. 149: 203-208) or (4) Robinson et al. (1990, Breast Cancer Res. Treat. 15: 95-101). The Office Action alleges that although the primary references do not teach hCG treatment in combination with Type 1 interferon, any one of Plantanias, Oberg, Recchia, or Robinson teach that Type 1 interferon has anti-tumor activity, and that it would have been obvious to use Type 1 interferon in combination with hCG. Applicants traverse the rejection.

As set forth above, the present invention is directed to a method of treating clinically manifest mammary tumors in postmenopausal women, and the primary references do not teach or suggest this method. The deficiencies in the primary references are not supplied by Plantanias, Oberg, Recchia, or Robinson. Plantanias, Oberg, Recchia, or Robinson do not teach or suggest that hCG could be used in combination with Type 1 interferon to treat clinically manifest mammary tumors in postmenopausal women. Thus, all of the limitations of the invention are not taught or suggested by the prior art, alone or in combination. In this regard, the skilled artisan would not be motivated to modify or combine any of these references, and would not have an expectation of success to arrive at the invention as claimed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 45, 55-58, 70-76, and 78 under 35 U.S.C. Section 103(a).

Claims 45, 55-58, 70-76, and 80 are rejected under 35 U.S.C. §103(a) as allegedly obvious over any one of (1) Srivastava et al. (1997, Carcinogenesis 18: 1799-1808); (2) Russo et al. (1990, J. Natl. Cancer Inst. 82: 1286-1289); or (3) Russo et al. (1990, Br. J. Cancer 62: 2343-2347), in view of the Sigma Chemical Co. catalog (1995, page 263). The Office Action alleges that although the primary references do not teach that the hCG used is recombinant, recombinant hCG is available through commercial suppliers such as Sigma Chemical Co., and that it would have been obvious to vary the presently claimed methods by using recombinant hCG. Applicants traverse the rejection.

As set forth above, the present invention is directed to a method of treating clinically manifest mammary tumors in postmenopausal women, and the primary references do not teach or suggest this method. The deficiencies in the primary references are not supplied by the Sigma Chemical Co. catalog (1995, page 263). The Sigma Chemical Co. catalog (1995, page 263) does not teach or suggest that recombinant hCG could be administered in a method to treat clinically manifest mammary tumors in postmenopausal women. Thus, all of the limitations of the invention are not taught or suggested by the prior art, alone or in combination. In this regard, the skilled artisan would not be motivated to modify or combine any of these references, and would not have an expectation of success to arrive at the invention as claimed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 45, 55-58, 70-76, and 80 under 35 U.S.C. Section 103(a).

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PATENT

Conclusion

In view of the amendments submitted herewith and the foregoing remarks, the presently pending claims are believed to be in condition for allowance. Applicants respectfully request early and favorable reconsideration and withdrawal of the objections and rejections set forth in the December 3, 2004 Official Action, and allowance of this application.

Respectfully submitted,



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